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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/538,985

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Moritz Bunemann

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EXAMINER

PAK, MICHAEL D

ART UNIT

PAPER NUMBER

1646

MAIL DATE

DELIVERY MODE

11/25/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/538,985	Applicant(s) BUNEMANN ET AL.	
	Examiner Michael Pak	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 July 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-31 is/are pending in the application.
- 4a) Of the above claim(s) 11-23 and 26-30 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-10, 24, 25 and 31 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Response to Amendment

1. Amendment filed July 6, 2009 has been entered.
2. Applicant's arguments filed July 6, 2009, have been fully considered but they are not found persuasive.
3. Claims 1-10, 24-25 and 31 are being examined. Claims 11-23 and 26-30 have been withdrawn.
4. This application contains claims 11-23 and 26-30 and in part claims 24-25 drawn to an invention nonelected with traverse in the reply filed on November 11, 2008. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Objections

5. Claims 24 and 25 is objected to because of the following informalities.
Appropriate correction is required.

Claims 24 and 25 are dependent on non-elected claims which is confusing and can only be examined in part.

Claim Rejections - 35 USC § 112

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The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-10, 24-25 and 31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims recite or encompass the amended claim terms "human or mouse G-protein receptor" or "human or mouse G-protein receptor" which is ambiguous and the metes and bounds of the terms are not clear. The claims are not limited by structural limitations and it is not clear when receptor is of human or mouse because the receptor have mutations which changes the structure of the receptor from the originally isolated receptor. Once the structure is changed then it is not clear which category the receptor belongs either mouse or human. The structural limitations which makes a receptor a mouse or a human is not known and the metes and bounds is not clear when a receptor meets these structural limitations.

Claims 9 and 10 recite or encompass the term "stringent hybridization conditions" which is a relative term whose metes and bounds are not clear. Applicants argue that specification on page 23 provide support for the claim amendments. However, the term is not defined in the specification on page 23. Furthermore, stringent hybridization

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conditions have specific temperature and salt conditions as well as washing conditions.

Claims 1-8 and 24-25 encompass the term.

7. Claims 1-10, 24-25 and 31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while enabling for a G-protein-coupled receptor using CFP and YFP to label both third intracellular loop and the carboxy-terminus, does not reasonably provide enablement for a seven-transmembrane receptor such as proto-oncogene labeled in both carboxy-terminus and third or first intracellular loop nor does not reasonably provide enablement for any G-protein coupled receptor labeled in both first cellular loop and carboxy-terminus. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The first paragraph of § 112 requires that the patent specification enable "those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation." Genentech, Inc. v. Novo Nordisk AIS, 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997) (quoting In re Wright, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)); see also In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). ("[T]he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art."). Whether making and using the invention would have required undue experimentation, and thus whether the disclosure is enabling is a legal conclusion based upon several underlying factual inquiries. See In re Wands, 858 F.2d

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731, 735, 736-37, 8 USPQ2d 1400, 1402, 1404 (Fed. Cir. 1988). As set forth in Wands, the factors to be considered in determining whether a claimed invention is enabled throughout its scope without undue experimentation include the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claims.

Likewise, in Amgen Inc. v. Chugai Pharm. Co., 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991), the court affirmed the holding of invalidity of claims to analogs of the EPO gene under § 112 for lack of enablement where applicants had claimed every possible analog of the EPO gene but had disclosed only how to make EPO and a very few analogs. "[D]espite extensive statements in the specification concerning all analogs of the EPO gene that can be made, there is little enabling disclosure of the particular analogs and how to make them There may be many other genetic sequences that code for EPO-type products. Amgen has told how to make and use only a few of them and is therefore not entitled to claim all of them." *Id.*, 927 F.2d at 1213-14, 18 USPQ2d at 1027.

Claims encompass all seven membrane receptor including proto-oncogene which is labeled in both carboxy-terminus and third or first intracellular loop. However, one skilled in the art cannot use all seven transmembrane receptor to label the third or first intracellular loop because unlike the G-protein coupled receptors, the labeling with large insert with fluorescent protein into the third intracellular loop or first intracellular

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loop will sterically disrupt the interaction with G-protein or other functional activator in the intracellular region. Furthermore claims encompass G-protein or other seven transmembrane receptor labeled with both carboxy terminus and first intracellular loop. However, the one skilled in the art cannot use receptors labeled in the first intracellular loop because the large fluorescent protein insert will disrupt the interaction with G-protein or other functional activator in the intracellular region. The amount of direction provided in the specification is limited to a specific species of G-protein coupled receptor with CFP and YFP inserted into third intracellular loop and the carboxy-terminus. One skilled in the art would require empirical experimentation in order to determine the effect of inserting CFP and YFP or other fluorescent proteins into other seven transmembrane receptors without disrupting the intracellular structure for the protein activity. Furthermore, one skilled in the art would require empirical experimentation in order to determine the effect of inserting fluorescent protein into the first intracellular loop without disrupting the intracellular structure due to steric hindrance or folding hindrance for the protein activity. The specification does not teach how to use such variant labeled receptors which are functional. Receptors have specific folding with active sites and intracellular active region which are essential for the proper function of the protein in functioning (Kobilka et al., *Methods in Enzymology*, 2002). The state of the art is such that one skilled in the art cannot predict the outcome of changes to protein structure using large fluorescent protein insertion into important structural domains. Thus, one skilled in the art cannot predict the functional outcome of the insertion of fluorescent protein into domains of the receptor. No working example is

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provided to determine whether a change in the first intracellular loop would provide proper function. It would require empirical experimentation to determine whether the variants is functional . Thus, such variants encompass a genus with a large number of species which are not functional. In view of the extent and the unpredictability of the experimentation required to practice the invention as claimed, one skilled in the art could not make the invention without undue experimentation. Therefore, based on the above Wands analysis, a preponderance of the evidence supports a conclusion that one skilled in the art would not have been enabled to make and use the claimed invention without undue experimentation.

Applicants argue that specific receptors have been shown to work with the third intracellular labeled in the FRET. However, the rejection is directed claims which encompass other intracellular region labeled for FRET analysis.

Applicants argue that the first intracellular loop has been labeled which functions to be activated by effector as shown on figure J. However, no figure J was found in the specification nor attached to applicant's arguments. Furthermore, the claims encompass not just the labeling of the receptor which functions to activate the receptor but must function in a FRET assay. No such data are available.

8. No claim is allowed.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

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§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Pak whose telephone number is 571-272-0879. The examiner can normally be reached on 8:00 - 2:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael Pak/
Primary Examiner, Art Unit 1646